AND PRELIMINARY AMENDMENT

Application No.: 10/575,261

**AMENDMENTS TO THE CLAIMS** 

This listing of claims will replace all prior versions and listings of claims in the

application:

LISTING OF CLAIMS:

1. (currently amended): A fusion protein composition comprising a fusion

protein molecule of a binding protein and an antibody Fc region having complex type

N-glycoside-linked sugar chains, wherein the complex type N-glycoside-linked sugar

chains have a structure in which fucose is not bound to N-acetylglucosamine in the

reducing end in the sugar chains, and wherein the binding protein comprises at least one

protein selected from the group consisting of a single chain antibody, a soluble receptor

and a ligand protein.

2. (original): The fusion protein composition according to claim 1, wherein the

complex type N-glycoside-linked sugar chains are sugar chains in which 1-position of fucose

is not bound to 6-position of N-acetylglucosamine in the reducing end through  $\alpha$ -bond in the

sugar chains.

3. (previously presented): The fusion protein composition according to claim 1,

wherein the antibody Fc region is an IgG class of a human antibody.

4. (original): The fusion protein composition according to claim 3, wherein the

2

AND PRELIMINARY AMENDMENT

Application No.: 10/575,261

antibody Fc region is an IgG1 class of a human antibody.

5. (original): The fusion protein composition according to claim 4, wherein the antibody fusion protein composition comprises an IgG1 class heavy chain constant region domain 2 (CH<sub>2</sub>) of a human antibody.

6. (original): The fusion protein composition according to claim 5, wherein the fusion protein composition comprises a hinge region, a heavy chain constant region domain 2 (CH<sub>2</sub>) and a heavy chain constant region domain 3 (CH<sub>3</sub>) of a human IgG1 class antibody.

## 7-12. (canceled).

- 13. (currently amended): The fusion protein composition according to claim 7claim 1, wherein the binding fragment of ansingle chain antibody is a bispecific single-chain antibody.
- 14. (currently amended): The fusion protein composition according to elaim 7-claim 1, wherein the soluble receptor is a soluble TNF (tumor necrosis factor) receptor II.
- 15. (currently amended): The fusion protein composition according to elaim 15 claim 14, wherein the soluble receptor comprises the amino acid sequence

AND PRELIMINARY AMENDMENT

Application No.: 10/575,261

represented by SEQ ID NO:64.

- 16. (previously presented): The fusion protein composition according to claim 14, wherein the fusion protein is produced by FERM BP-8499.
- 17. (currently amended): The fusion protein composition according to claim 7claim 1, wherein the ligand protein is LFA-3 (leukocyte function antigen-3).
- 18. (currently amended): The fusion protein composition according to elaim 16claim 17, wherein the ligand protein comprises the amino acid sequence represented by SEQ ID NO:65.
- 19. (previously presented): The fusion protein composition according to claim 17, wherein the fusion protein is produced by FERM BP-8500.
- 20. (previously presented): The fusion protein composition according to claim 1, wherein the fusion protein composition is a dimer.
- 21. (previously presented): A transformant obtainable by introducing a DNA encoding the fusion protein according to claim 1 into a host cell.

AND PRELIMINARY AMENDMENT

Application No.: 10/575,261

22. (original): The transformant according to claim 21, wherein the host cell is a cell in which a genome is modified so that an enzyme relating to synthesis of an intracellular sugar nucleotide, GDP-fucose or an enzyme relating to a modification of a sugar chain in which 1-position of fucose is bound to 6-position of N-acetylglucosamine in the reducing end through a-bond in the complex type N-glycoside-linked sugar chain is inactivated.

- 23. (original): The transformant according to claim 22, wherein the host cell is a cell in which all of alleles on a genome encoding an enzyme relating to synthesis of an intracellular sugar nucleotide, GDP-fucose or an enzyme relating to a modification of a sugar chain in which 1-position of fucose is bound to 6-position of N-acetylglucosamine in the reducing end through α-bond in the complex type N-glycoside-linked sugar chain are knocked out.
- 24. (previously presented): The transformant according to claim 22, wherein the enzyme relating to synthesis of an intracellular sugar nucleotide, GDP-fucose, is an enzyme selected from the group consisting of GDP-mannose 4,6-dehydratase (GMD) and GDP-4-keto-6-deoxy-D-mannose 3,5-epimerase (Fx).
- 25. (original): The transformant according to claim 24, wherein the GDP-mannose 4.6-dehydratase is a protein encoded by a DNA selected from the following (a) or (b):
  - (a) a DNA comprising the nucleotide sequence represented by SEQ ID NO:1;

AND PRELIMINARY AMENDMENT

Application No.: 10/575,261

(b) a DNA which hybridizes with a DNA consisting of the nucleotide sequence represented by SEQ ID NO:1 under stringent conditions and which encodes a protein having GDP-mannose 4,6-dehydratase activity.

- 26. (original): The transformant according to claim 24, wherein the GDP-mannose 4,6-dehydratase is a protein selected from the group consisting of the following (a), (b) and (c):
  - (a) a protein comprising the amino acid sequence represented by SEQ ID NO:2;
- (b) a protein consisting of an amino acid sequence wherein one or more amino acid(s) is/are deleted, substituted, inserted and/or added in the amino acid sequence represented by SEQ ID NO:2 and having GDP-mannose 4,6-dehydtratase activity;
- (c) a protein consisting of an amino acid sequence which has 80% or more homology to the amino acid sequence represented by SEQ ID NO:2 and having GDP-mannose 4.6-dehydratase activity.
- 27. (original): The transformant according to claim 24, wherein the GDP-4-keto-6-deoxy-D-mannose 3,5-epimerase is a protein encoded by a DNA selected from the following (a) or (b):
  - (a) a DNA comprising the nucleotide sequence represented by SEQ ID NO:3;
- (b) a DNA which hybridizes with a DNA consisting of the nucleotide sequence represented by SEQ ID NO:3 under stringent conditions and which encodes a protein having

AND PRELIMINARY AMENDMENT

Application No.: 10/575,261

GDP-4-keto-6-deoxy-D-mannose 3,5-epimerase activity.

**28.** (original): The transformant according to claim 24, wherein the GDP-4-keto-6-deoxy-D-mannose 3,5-epimerase activity is a protein selected from the group consisting of the following (a) to (c):

- (a) a protein comprising the amino acid sequence represented by SEQ ID NO:4;
- (b) a protein consisting of an amino acid sequence wherein one or more amino acid(s) is/are deleted, substituted, inserted and/or added in the amino acid sequence represented by SEQ ID NO:4 and having GDP-4-keto-6-deoxy-D-mannose 3,5-epimerase activity;
- (c) a protein consisting of an amino acid sequence which has 80% or more homology to the amino acid sequence represented by SEQ ID NO:4 and having G GDP-4-keto-6-deoxy-D-mannose 3,5-epimerase activity.
- 29. (previously presented): The transformant according to claim 22, wherein the enzyme relating to a modification of a sugar chain in which 1-position of fucose is bound to 6-position of N-acetylglucosamine in the reducing end through  $\alpha$ -bond in the complex type N-glycoside-linked sugar chain is  $\alpha$ 1,6-fucosyltransferase.
- 30. (original): The transformant according to claim 29, wherein the  $\alpha$  1,6-fucosyltransferase is a protein encoded by a DNA selected from the group consisting of the following (a) to (d):

AND PRELIMINARY AMENDMENT

Application No.: 10/575,261

(a) a DNA comprising the nucleotide sequence represented by SEQ ID NO:5;

- (b) a DNA comprising the nucleotide sequence represented by SEQ ID NO:6;
- (c) a DNA which hybridizes with a DNA consisting of the nucleotide sequence represented by SEQ ID NO:5 under stringent conditions and which encodes a protein having α1,6-fucosyltransferase activity;
- (d) a DNA which hybridizes with a DNA consisting of the nucleotide sequence represented by SEQ ID NO:6 under stringent conditions and which encodes a protein having α1,6-fucosyltransferase activity.
- 31. (original): The transformant according to claim 29, wherein the  $\alpha$ 1,6-fucosyltransferase is a protein selected from the group consisting of the following (a) to (f):
  - (a) a protein comprising the amino acid sequence represented by SEQ ID NO:7;
  - (b) a protein comprising the amino acid sequence represented by SEQ ID NO:8;
- (c) a protein consisting of an amino acid sequence wherein one or more amino acid(s) is/are deleted, substituted, inserted and/or added in the amino acid sequence represented by SEQ ID NO:7 and having α 1,6-fucosyltransferase activity;
- (d) a protein consisting of an amino acid sequence wherein one or more amino acid(s) is/are deleted, substituted, inserted and/or added in the amino acid sequence represented by SEQ ID NO:8 and having α 1,6-fucosyltransferase activity;
- (e) a protein consisting of an amino acid sequence which has 80% or more homology to the amino acid sequence represented by SEQ ID NO:7 and having

AND PRELIMINARY AMENDMENT

Application No.: 10/575,261

 $\alpha$ 1,6-fucosyltransferase activity;

(f) a protein consisting of an amino acid sequence which has 80% or more homology to the amino acid sequence represented by SEQ ID NO:8 and having α1.6-fucosyltransferase activity.

- 32. (previously presented): The transformant according to claim 21, wherein the host cell is a cell selected from the group consisting of the following (a) to (h):
  - (a) a CHO cell derived from Chinese hamster ovary tissue;
  - (b) a rat myeloma cell line YB2/3HL.P2.G11.16Ag.20 cell;
  - (c) a mouse myeloma cell line NSO cell;
  - (d) a mouse myeloma cell line SP2/0-Ag14 cell;
  - (e) a BHK cell derived from Syrian hamster kidney tissue;
  - (f) a human leukemia cell line Namalwa cell;
  - (g) an embryonic stem cell;
  - (h) a fertilized egg cell.
- 33. (previously presented): The transformant according to claim 21, wherein the transformant is FERM BP-8499.
- 34. (previously presented): The transformant according to claim 21, wherein the transformant is FERM BP-8500.

AND PRELIMINARY AMENDMENT

Application No.: 10/575,261

35. (currently amended): A process for producing the fusion protein composition according to any one of claims 1 to 20, which comprises culturing transformant a transformant obtainable by introducing a DNA encoding the fusion protein according to claim 1 into a host cell, in a medium to form and accumulate the fusion protein composition in the culture and recovering and purifying the fusion protein composition from the culture.

- 36. (currently amended): The fusion protein according to claim 1 obtained by a process comprising culturing a transformant with DNA encoding said fusion protein in medium to form and accumulate said fusion protein in culture, and recovering and purifying the antibody from the culture, which is obtainable by the process according to claim 35.
- 37. (previously presented): A medicament comprising the fusion protein composition according to claim 1 and a pharmaceutically acceptable carrier.
- 38. (previously presented): A method for preventing or treating tumor, inflammatory diseases or autoimmune diseases, comprising administering to a subject in need thereof an effective amount of the fusion protein composition according to claim 1.
  - 39. (previously presented): The method according to claim 38, wherein the tumor

AND PRELIMINARY AMENDMENT
Application No.: 10/575,261

is blood tumor or cancer.